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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/083,424	02/26/2002	Jin-Kyoo Kim	5294-000006	6744

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EXAMINER
BASKAR, PADMAVATHI

ART UNIT	PAPER NUMBER
1645	9

DATE MAILED: 09/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/083,424	Applicant(s) KIM ET AL.	
	Examiner Padmavathi v Baskar	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sh t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 7, 13 in part and claim 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-22* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2a .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continuation of Disposition of Claims: Claims withdrawn from consideration are 1, 2, in part, 3-6, 7 in part, 9-11, and 12, 13 in part and 14 -22.

DETAILED ACTION

1. The Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1645.

2. Applicant's preliminary amendment filed on 2/26/02 is entered. Claims 21 and 22 have been amended. Claims 1-22 are pending in the application.

Priority

3. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) to

Priority Document	Date	Country
2001-52934	08/30/2001	REPUBLIC OF KOREA

Information Disclosure Statement

4. The Information Disclosure Statement filed on 2/26/02 is acknowledged and a signed copy of the same is enclosed with this office action.

Election

5. Applicant's election of Group V, Claims 1, 2, 7, 13 (in part with respect to SEQ.ID.NO: 18 and SEQ.ID.NO: 26) and 8 in Paper No.8 (8/25/03) with traverse is acknowledged.

It is noted that the elected invention is Group V, Claims 1, 2, 7, 13 (in part with respect to SEQ.ID.NO: 18 and SEQ.ID.NO: 26) and 8, and not claim 12 as applicant indicated in Paper # 8.

Applicant requests the examiner to reconsider the restriction requirement and examine all groups. The traversal is on the ground(s) that all groups are drawn to same subject matter and is not undue burden upon the examiner.

This is not found persuasive because (1) applicant has not shown how these proteins are integrally related and to what? In the instant case the different inventions represent structurally different polypeptides and the polynucleotides encoding them. The examiner would like to bring applicant's attention to Paper # 7, paragraph 2 in which the examiner indicated patentably distinct inventions that are different to each other ins structure, property and function.

Further, the restriction of different inventions with different sequences requires independent searches. The search for each of the above inventions is not co-extensive particularly with regard to the literature search. A reference, which would anticipate the invention of one SEQ.ID.NO, would not necessarily anticipate or make obvious any of the other SEQ.ID.NOS. Moreover, as to the question of burden of search, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Burden in examining materially different groups having materially different issues also exists. Restriction is deemed proper and therefore, claims 1, 2, with respect to SEQ.ID.NOS: 20, 22, 24, 38, 28, 30, 32, and 40, Claims 3-6, 7 with respect to SEQ.ID.NOS: 20, 22, 24, 38, 28, 30, 32, and 40, claims 9-11, and claims 12, 13 with respect to SEQ.ID.NOS: 20, 22, 24, 38, 28, 30, 32, and 40 and Claims14 -22 are withdrawn from consideration.

Applicant is advised to amend the claims 1, 2, 7 and 13 to elected invention i.e., SEQ.ID.NO: 18 and SEQ.ID.NO: 26.

Claim Rejections - 35 USC 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying

7. Claims 1, 2, 7, 13 in part and claim 8 are rejected under 35 U.5.C. 112, first paragraph,

as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is referred to the interim guidelines on written description published June 15, 1998 in the Federal Register at Volume 63, Number 114, pp 32639-32645 (also available at www.uspto.gov). This is a written description rejection.

Claims 1and 2 are drawn to a heavy chain variable region of an antibody specific to a surface antigen in sporozoites of Eimeria spp., which comprises an amino acid sequence SEQ.ID.NO: 18 and a light chain variable region of an antibody specific to a surface antigen in sporozoites of Eimeria spp., which comprises an amino acid sequence SEQ.ID.NO: 26.

Claims 7, 8 and 13 are drawn to a recombinant scFv antibody specific to a surface antigen in sporozoites of Eimeria spp., which comprises (a) a heavy chain variable region of an antibody specific to a surface antigen in sporozoites of Eimeria spp., which comprises an amino acid sequence SEQ.ID.NO: 18 (b) a light chain variable region of an antibody specific to a surface antigen in sporozoites of Eimeria spp., which comprises an amino acid sequence SEQ.ID.NO: 26, wherein scFv antibody comprises a linker between heavy chain region and the light chain variable region.

The specification describes (pages 26-37) that total RNA was purified from chicken B-cell hybridoma 2-1 and heavy and light chains were amplified and sequenced. Using cDNA of variable regions obtained from 2-1 cell line, overlap-extension PCR was carried out to amplify genes of recombinant variable regions (variable heavy chain SEQ.ID.NO: 18 and light chain variable SEQ.ID.NO: 26). VL- GS linker-VH (LH construct) and VH-GS linker-VL gene (HL construct) were amplified through PCR using purified VL and VH genes. PCR products were digested and cloned into scFv expression vector and scFv antibodies were purified. This

antibody was characterized using sprozoite antigen approximately12kD from *Eimeria aeruvulina* as part of the invention. The specification teaches that antibodies 2-1 LH were reactive to only sporozoites antigen of *Eimeria aeruvulina* as determined by ELISA in figure 8. However, the specification does not teach

1. a heavy chain variable region comprising an amino acid sequence SEQ.ID.NO: 18 that binds to an antibody specific to a surface antigen in sporozoites of Eimeria spp.,

2. a light chain variable region comprising an amino acid sequence SEQ.ID.NO: 26 binds to an antibody specific to a surface antigen in sporozoites of Eimeria spp.,

3. a recombinant scFv antibody specific to all surface antigens of sporozoites of all Eimeria spp., which comprises (a) a heavy chain variable region of an antibody specific to a surface antigen in sporozoites of all Eimeria spp., which comprises an amino acid sequence SEQ.ID.NO: 18 (b) a light chain variable region of an antibody specific to a surface antigen in sporozoites of Eimeria spp., which comprises an amino acid sequence SEQ.ID.NO: 26, wherein scFv antibody comprises a linker between heavy chain region and the light chain variable region.

Applicants broadly describe the invention as embracing any sporozoite antigen from any Eimeria species, which would bind to heavy chain alone or light, chain alone or any sprozoite antigen from any species, which would bind to the disclosed scFv antibody. USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116).

The specification fails to teach that a heavy chain by itself and light chain by itself bind to sporozoite antigen of all species of genus Eimeria. It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody (Rudikoff et al, Proc Natl Acad Sci USA 1982, Vol 79 page 1979). It is noted that the applicant's specification teaches that scFv antibody to LH was reactive to *Eimeria aeruvulina* antigen and that of scFv antibody to HL was non-reactive to *E. aeruvulina* antigen (see page 47, second paragraph and figure 8). The art indicates that animals infected with various species of Eimeria produce i.e., *E.tenella, E.maxima, E.mitis, E.necatrix, E.brunetti E.praecox* parasite specific antibodies (see review article by Lillehoj et al 1996 page 355 under humoral immune response). Further the art indicates that the antigen specificity of the antibodies to these parasites, *E.tenella, E.maxima, E.mitis, E.necatrix, E.brunetti E.praecox is* extremely complex.

The specification fails to teach the structure or relevant identifying characteristics of a antibody that bind to any sporozoite antigens from any species of Eimeria which include *E.tenella, E.maxima, E.mitis, E.necatrix, E.brunetti E.praecox* etc, sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 U5PQ2d 1601, 1606 (CAFC 1993) and Amgen Inc V Chugai Pharmaceutical Co Ltd., 18 U5PQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 U5PQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. Therefore, (1) an Sc Fv antibody specifically binds to E. *aeruvulina* sporozoite 12kD antigen comprising the heavy chain variable region as set forth in the amino acid sequence SEQ.ID.NO: 18 and a light chain variable region comprising the amino acid sequence SEQ.ID.NO: 26, and (2) a recombinant

scFv antibody specific to a sporozoite surface antigen 12 kD from *Eimeria aeruvulina*, which comprises a heavy chain variable region comprising the amino acid sequence SEQ.ID.NO: 18, a light chain variable region comprising the amino acid sequence SEQ.ID.NO: 26, wherein scFv antibody comprises a linker between light chain region and the heavy chain variable region meet the written description provision of 35 U.S.C. 112, first paragraph for the reasons set forth as above.

8. Claims 1, 2, 7, 13 in part and claim 8 are also rejected under 35 U.5.C. 112, first paragraph, because the specification, while being enabling for an Sc Fv antibody which specifically binds to E. *aeruvulina* sporozoite 12kD antigen comprising the heavy chain variable region as set forth in the amino acid sequence SEQ.ID.NO: 18 and a light chain variable region comprising the amino acid sequence SEQ.ID.NO: 26, and (2) a recombinant scFv antibody specific to a sporozoite surface antigen 12 kD from *Eimeria aeruvulina*, which comprises a heavy chain variable region comprising the amino acid sequence SEQ.ID.NO: 18, a light chain variable region comprising the amino acid sequence SEQ.ID.NO: 26, wherein scFv antibody comprises a linker between light chain region and the heavy chain variable region does not reasonably provide enablement for (1)a heavy chain variable region of an antibody specific to a surface antigen of sporozoites of Eimeria spp., which comprises an amino acid sequence SEQ.ID.NO: 18, (2) a light chain variable region of an antibody specific to a surface antigen in sporozoites of Eimeria spp., which comprises an amino acid sequence SEQ.ID.NO: 26 and (3) a recombinant scFv antibody specific a surface antigen in sporozoites of Eimeria spp., which comprises (a) a heavy chain variable region of an antibody specific to a surface antigen of sporozoite of Eimeria spp., which comprises an amino acid sequence SEQ.ID.NO: 18 (b) a light chain variable region of an antibody specific to a surface antigen in sporozoites of Eimeria spp., which comprises an amino acid sequence SEQ.ID.NO: 26 , wherein scFv antibody comprises a

linker between heavy chain region and the light chain variable region. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity, which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 1982 Vol 79 page 1979). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. It is unlikely that the protein of heavy chain variable region and light chain variable region as defined by the claims which may contain less than the full complement of CDRs from the heavy and light chain variable regions of ScFv antibody in unspecified order having the required binding function to sporozoite antigen. The specification provides no direction or guidance regarding how to produce antibodies as broadly defined by the claims. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

The art indicates that animals infected with various species of Eimeria produce i.e., *E.tenella, E.maxima, E.mitis, E.necatrix, E.brunetti E.praecox* parasite specific antibodies (see review article by Lillehoj et al 1996 page 355 under humoral immune response). Further the art indicates that the antigen specificity of the antibodies to these parasites, *E. tenella, E. maxima, E. mitis, E. necatrix, E. brunetti and E.praecox is* extremely complex.

Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention as it pertains to.

Status of Claims

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

9/17/03

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9/23/03